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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,998	04/13/2001	Roberto A. Gaxiola	0399.2004-002	4319
21005	7590	12/22/2003	EXAMINER	
HAMILTON, BROOK, SMITH & REYNOLDS, P.C. 530 VIRGINIA ROAD P.O. BOX 9133 CONCORD, MA 01742-9133			COLLINS, CYNTHIA E	
			ART UNIT	PAPER NUMBER
			1638	

DATE MAILED: 12/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/834,998	GAXIOLA ET AL.	
<b>Examiner</b>	<b>Art Unit</b>		
Cynthia Collins	1638		

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 23 September 2003.

2a)  This action is **FINAL**.                            2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## **Disposition of Claims**

4)  Claim(s) 1-76 is/are pending in the application.  
4a) Of the above claim(s) 1-64 and 74-76 is/are withdrawn from consideration.  
5)  Claim(s) \_\_\_\_\_ is/are allowed.  
6)  Claim(s) 65-73 is/are rejected.  
7)  Claim(s) \_\_\_\_\_ is/are objected to.  
8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on 13 April 2001 is/are: a)  accepted or b)  objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)  The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a)  All b)  Some \* c)  None of:  
1.  Certified copies of the priority documents have been received.  
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

13)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a)  The translation of the foreign language provisional application has been received.

14)  Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

1)  Notice of References Cited (PTO-892) 4)  Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_  
2)  Notice of Draftsperson's Patent Drawing Review (PTO-948) 5)  Notice of Informal Patent Application (PTO-152)  
3)  Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_. 6)  Other: \_\_\_\_\_

**DETAILED ACTION**

***Election/Restrictions***

Applicant's election without traverse of Group VIII, claims 65-73, filed September 23, 2003, is acknowledged.

***Information Disclosure Statement***

An initialed and dated copy of Applicant's IDS form 1449, filed August 29, 2002, is attached to the instant Office action.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 65-73 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a transgenic plant which is tolerant to a salt, said plant comprising one or more plant cells transformed with any type of exogenous nucleic acid which alters in any way, including increasing or downregulating, the expression of any vacuolar pyrophosphatase, including AVP1 or a homologue thereof, including homologues from tobacco,

bacteria, tomato or corn, and which alters in any way the expression of any  $\text{Na}^+/\text{H}^+$  antiporter, including *NtNHX1* or a homologue thereof, in the plant. The claims are also drawn to transgenic progeny of the transgenic plant of claim 65, seeds produced by the transgenic plant of claim 65, and a progeny transgenic plant grown from the seed of claim 72.

While the specification does not describe any salt tolerant transgenic plant transformed with a single exogenous nucleic acid which alters both the expression of a vacuolar pyrophosphatase and a  $\text{Na}^+/\text{H}^+$  antiporter, the specification does describe two types of salt tolerant transgenic plants each transformed with a single nucleic acid construct which encodes and expresses either the *Arabidopsis* vacuolar pyrophosphatase *AVP1* or the *Arabidopsis*  $\text{Na}^+/\text{H}^+$  antiporter *AtNHX1* (26-27). The specification also describes a method of making salt tolerant transgenic plants comprising a nucleic acid construct which encodes and expresses the *Arabidopsis* vacuolar pyrophosphatase *AVP1* and a nucleic acid construct which encodes and expresses the *Arabidopsis*  $\text{Na}^+/\text{H}^+$  antiporter *AtNHX1* (27-29).

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that “A description of a genus of cDNAs may be achieved by means of recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus.” See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1569; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In the instant case Applicant has not described a representative number of species falling within the scope of the claimed genus, nor the structural features unique to the genus. The specification does not describe salt tolerant transgenic plants transformed with exogenous nucleic acids

encoding other vacuolar pyrophosphatases or other Na+/H<sup>+</sup> antiporters. The specification also does not describe salt tolerant transgenic plants transformed with an exogenous nucleic acid which downregulates the expression of a vacuolar pyrophosphatase and/or a Na+/H<sup>+</sup> antiporter. Additionally, the specification does not describe salt tolerant transgenic plants transformed with exogenous nucleic acids encoding AVP1 homologues or AtNHX1 homologues. More specifically, the specification does not describe AVP1 homologues from tobacco, bacteria, tomato or corn.

Claims 65-73 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic plant which is tolerant to sodium chloride and which comprises two nucleic acid constructs, one which encodes and increases the expression of the *Arabidopsis* vacuolar pyrophosphatase AVP1 and one which encodes and increases the expression of the *Arabidopsis* Na+/H<sup>+</sup> antiporter AtNHX1, does not reasonably provide enablement for a transgenic plant which is tolerant to any other salt, or which is transformed with any other types of exogenous nucleic acid which alters in any way the expression of any vacuolar pyrophosphatase and which alters in any way the expression of any Na+/H<sup>+</sup> antiporter. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to a transgenic plant which is tolerant to any salt, said plant comprising one or more plant cells transformed with any type of exogenous nucleic acid which alters in any way, including increasing or downregulating, the expression of any vacuolar

pyrophosphatase, including AVP1 or a homologue thereof, including homologues from tobacco, bacteria, tomato or corn, and which alters in any way the expression of any  $\text{Na}^+/\text{H}^+$  antiporter, including NtNHX1 or a homologue thereof, in the plant. The claims are also drawn to transgenic progeny of the transgenic plant of claim 65, seeds produced by the transgenic plant of claim 65, and a progeny transgenic plant grown from the seed of claim 72.

The specification discloses a salt tolerant transgenic plant transformed with a nucleic acid construct which encodes and expresses the *Arabidopsis* vacuolar pyrophosphatase AVP1, and a salt tolerant transgenic plant transformed with a nucleic acid construct which encodes and expresses the *Arabidopsis*  $\text{Na}^+/\text{H}^+$  antiporter AtNHX1 (26-27). The specification also discloses how to make a salt tolerant transgenic plant which comprises two nucleic acid constructs, one which encodes and expresses the *Arabidopsis* vacuolar pyrophosphatase AVP1 and one which encodes and expresses the *Arabidopsis*  $\text{Na}^+/\text{H}^+$  antiporter AtNHX1, by crossing the transgenic plants transformed with the single nucleic acid constructs (27-29).

The specification does not, however, disclose how to make and use a salt tolerant transgenic plant transformed with a single nucleic acid construct which simultaneously alters both the expression of a vacuolar pyrophosphatase and the expression of a  $\text{Na}^+/\text{H}^+$  antiporter, or which downregulates the expression of a vacuolar pyrophosphatase and/or a  $\text{Na}^+/\text{H}^+$  antiporter. The specification also does not disclose how to make and use transgenic plants that are tolerant to salts other than sodium chloride. The specification additionally does not disclose how to make and use a salt tolerant transgenic plant transformed with nucleic acid constructs encoding vacuolar pyrophosphatases other than AVP1 or encoding  $\text{Na}^+/\text{H}^+$  antiporters other than AtNHX1.

The specification does not provide sufficient guidance for one skilled in the art to make and/or use the full scope of the claimed invention without undue experimentation because the effect of expressing a nucleic acid construct designed to decrease the expression of a gene such as a vacuolar pyrophosphatase or a Na<sup>+</sup>/H<sup>+</sup> antiporter is unpredictable. The effect is unpredictable because multiple variables, such as the size and relative position of an antisense transcript, affect the ability of a nucleic acid to alter gene expression. See for example Sandler et al. (Plant Molecular Biology, 1988, Vol. 11, No. 3, pages 301-310), who teach that DNA fragments encoding different portions of the nopaline synthase gene, when expressed as antisense transcripts, vary in their ability to inhibit nopaline synthase gene expression; antisense transcripts downstream from the Cla I site (nucleotide 373) effectively suppressed nopaline synthase gene expression, whereas the full length antisense transcript and the antisense transcript upstream from the Cla I site (nucleotides 1 to 373) did not (page 308 column 2 and Table 4, page 309 column 1 first full paragraph). See also for example van der Krol et al. who teach a method of decreasing the expression of an endogenous petunia chalcone synthase gene by transforming petunia cells with chimeric genes comprising chalcone synthase (CHS) coding sequences operably linked in an antisense orientation to a CaMV 35S constitutive promoter (Plant Molecular Biology, 1990, Vol. 14, pages 457-466). The full length CHS cDNA and CHS sequences encoding half-length or quarter-length RNA complementary to the 3' half of the CHS mRNA decreased the expression of endogenous CHS, whereas half-length RNA complementary to the 5' half of the CHS mRNA did not (page 460 Figures 1 and 2; page 461 Figure 3). In the instant case Applicant has not provided guidance concerning how to make and use a nucleic acid

construct designed to alter the expression of a vacuolar pyrophosphatase and a  $\text{Na}^+/\text{H}^+$  antiporter by antisense or by any other mechanism.

The specification also does not provide sufficient guidance for one skilled in the art to make and/or use the full scope of the claimed invention without undue experimentation because conferring salt tolerance to a plant by expressing a nucleic acid construct designed to decrease the expression of a gene such as a vacuolar pyrophosphatase or a  $\text{Na}^+/\text{H}^+$  antiporter is unpredictable. The effect is unpredictable because opposite phenotypic effects are ordinarily observed between plants having increased and decreased expression of the same gene. The specification discloses that increasing the expression of the coding sequence of AVP1 or NHX1 increases plant salt tolerance, but the specification does not disclose that decreasing the expression of AVP1 or NHX1 also increases plant salt tolerance. Absent further guidance such a disclosure would indicate that decreasing the expression of AVP1 or NHX1 would in fact decrease plant salt tolerance. In the instant case Applicant has not provided further guidance concerning how to make and use salt tolerant transgenic plants transformed with a nucleic acid construct designed to decrease the expression of a gene such as a vacuolar pyrophosphatase or a  $\text{Na}^+/\text{H}^+$  antiporter.

Additionally, the specification does not provide sufficient guidance for one skilled in the art to make and/or use the full scope of the claimed invention without undue experimentation because conferring tolerance to any salt by expressing a nucleic acid construct designed to alter the expression of a gene such as a vacuolar pyrophosphatase or a  $\text{Na}^+/\text{H}^+$  antiporter is unpredictable. Conferring tolerance to any salt is unpredictable because a correlation between the activities of AVP1 and AtNHX1 and salts other than sodium chloride has not been established.

In the absence of further guidance undue experimentation would be required by one skilled in the art to show how the transport of other salts would be affected by altering, in any and all manners, the expression of any vacuolar pyrophosphatase and any  $\text{Na}^+/\text{H}^+$  antiporter in plants. Further, the specification does not enable transgenic plants in which the expression of a vacuolar pyrophosphatase and a  $\text{Na}^+/\text{H}^+$  antiporter are altered by other types of exogenous nucleic acids. For example, the specification does not teach nucleic acids whose products regulate the activities of a vacuolar pyrophosphatase and a  $\text{Na}^+/\text{H}^+$  antiporter. In the absence of further guidance, undue experimentation would be required by one skilled in the art to determine and isolate other types of nucleic acids that affect vacuolar pyrophosphatase and a  $\text{Na}^+/\text{H}^+$  antiporter expression. While the specification teaches that plants transformed with and expressing a nucleic acid construct encoding AVP1 or AtNHX1 are tolerate to sodium chloride, the specification provides no guidance with respect to the type or amount of other salts that would be tolerated by said plants.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 71-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are drawn to transgenic progeny of the transgenic plant of claim 65, seeds produced by the transgenic plant of claim 65, and a progeny transgenic plant grown from the seed of claim 72. It is unclear from the claims whether the claimed seeds and progeny comprise the exogenous nucleic acid used to transform the transgenic plant of claim 65, as the

seeds and progeny of a transgenic parent plant may or may not comprise the exogenous nucleic acid used to transform the parent plant. While claims 71 and 73 refer to the progeny as being "transgenic", they do not specify what the progeny are transgenic for, and claim 72 does not require that the produced seed be transgenic at all. Additionally, the rejected claims make no reference to the salt tolerant phenotype that would be conferred by the exogenous nucleic acid used to transform the transgenic plant of claim 65. In order to overcome the rejection, it is suggested that the claims be amended to indicate that the claimed seed and progeny comprise the exogenous nucleic acid used to transform the transgenic plant of claim 65. For example, a limitation such as -- wherein said progeny (or seeds) has said exogenous nucleic acid -- could be added to the claims.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 71-73 are rejected under 35 U.S.C. 102(a) as being anticipated by Apse et al.

(Science, 20 August 1999, Vol. 285, pages 1256-1258, Applicant's IDS).

The claims are drawn to transgenic progeny of the transgenic plant of claim 65, seeds produced by the transgenic plant of claim 65, and a progeny transgenic plant grown from the seed of claim 72.

Apse et al. teach seed produced by *Arabidopsis* plants transformed with a gene construct comprising the Na<sup>+</sup>/H<sup>+</sup> antiporter AtNHX1 (page 1258 Figure 3; page 1257 column 2). While Apse et al. do not teach the transgenic plant of claim 65, the seed taught by Aspe necessarily anticipate the claimed seed, as the rejected claims require only that the seed or progeny i) be transgenic for some unspecified transgene(s), ii) be produced by the transgenic plant of claim 65, and iii) be capable of growing into a transgenic plant transgenic for some unspecified transgene(s). The rejected claims do not require that the progeny or seed retain all or any of the parental transgenes. At least some of the seed taught by Aspe et al. would comprise an AtNHX1transgene, and at least some of the seed is presumed to be capable of growing into a transgenic plant, as development of the transgenic plants taught by Aspe et al. was reportedly not compromised since the transgenic plants bolted and set seed in all salt treatments.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 65-66 and 68-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Apse et al. (Science, 20 August 1999, Vol. 285, pages 1256-1258, Applicant's IDS) in view of Gaxiola et al. (PNAS, February 1999, Vol. 96, pages 1480-1485, Applicant's IDS), and in further view of Applicant's admitted prior art.

The claims are drawn to a transgenic plant which is tolerant to a salt, said plant comprising one or more plant cells transformed with an exogenous nucleic acid which alters the expression of a vacuolar pyrophosphatase, including AVP1 or a homologue thereof operably linked to a double tandem enhancer of the 35S promoter of CaMV, and a Na<sup>+</sup>/H<sup>+</sup> antiporter, including NtNHX1 or a homologue thereof, in the plant. The claims are also drawn to transgenic progeny of the transgenic plant of claim 65, seeds produced by the transgenic plant of claim 65, and a progeny transgenic plant grown from the seed of claim 72.

Apse et al. teach salt tolerant transgenic Arabidopsis plants transformed with an exogenous nucleic acid which alters the expression of the Arabidopsis Na<sup>+</sup>/H<sup>+</sup> antiporter AtNHX1 (page 1258 Figure 3).

Apse et al. do not teach salt tolerant transgenic Arabidopsis plants transformed with an exogenous nucleic acid which additionally alters the expression of a vacuolar pyrophosphatase.

Gaxiola et al. teach an exogenous nucleic acid which alters the expression of the Arabidopsis vacuolar pyrophosphatase AVP1 and which confers salt tolerance to the salt sensitive ena1 mutant of *Saccharomyces cerevisiae* (page 1481 Figure 1). Gaxiola et al. further teach that overexpression of AVP1 confers salt tolerance to yeast only in strains containing a functional chloride channel (Gef1) and Na<sup>+</sup>/H<sup>+</sup> exchanger (Nhx1) (page 1481 Figure 1; page 1482 column 2 first full paragraph; page 1484 column 1 first paragraph).

The specification teaches at page 26 lines 20-22 that use of the double tandem enhancer of the 35S promoter of CaMV in plant transformation constructs was known in the art prior to Applicant's invention.

Given the success of Apse et al. in making salt tolerant transgenic *Arabidopsis* plants transformed with an exogenous nucleic acid which alters the expression of AtNHX1, and given the teachings of Gaxiola et al. that the *Arabidopsis* vacuolar pyrophosphatase AVP1 can confer salt tolerance to salt sensitive yeast transformed therewith, it would have been obvious to further transform the transgenic plants taught by Apse et al. with the exogenous nucleic acid encoding AVP1 taught by Gaxiola et al., especially given the further teaching of Gaxiola et al. that overexpression of AVP1 confers salt tolerance to yeast only in strains containing a functional  $\text{Na}^+/\text{H}^+$  exchanger, without any surprising or unexplained results. Furthermore, the use of the double tandem enhancer of the 35S promoter of CaMV would have been an obvious modification of design parameters. Accordingly, one skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Claims 65-66 and 68-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheveleva et al. (Plant Physiology, 1997, Vol. 115, pages 1211-1219) in view of Barkla et al. (Plant Physiology, 1995, Vol. 109, pages 549-556), Sarafian et al. (PNAS, March 1992, Vol. 89, pages 1775-1779, Applicant's IDS), and Nass et al. (Journal of Biological Chemistry, 17 October 1997, Vol. 272, No. 42, pages 26145-26152), and in further view of Applicant's admitted prior art.

The claims are drawn to a transgenic plant which is tolerant to a salt, said plant comprising one or more plant cells transformed with an exogenous nucleic acid which alters the

expression of a vacuolar pyrophosphatase, including AVP1 or a homologue thereof operably linked to a double tandem enhancer of the 35S promoter of CaMV, and a Na<sup>+</sup>/H<sup>+</sup> antiporter, including NtNHX1 or a homologue thereof, in the plant. The claims are also drawn to transgenic progeny of the transgenic plant of claim 65, seeds produced by the transgenic plant of claim 65, and a progeny transgenic plant grown from the seed of claim 72.

Sheveleva et al. teach a transgenic plant which is tolerant to a salt and which is transformed with an exogenous nucleic acid which alters the expression of an enzyme (IMT1) whose activity is correlated with salt stress tolerance in plants (page 1214 Table 1; page 1215 Figure 4; page 1216 Table II).

Sheveleva et al. do not teach a transgenic plant which is tolerant to a salt and which is transformed with an exogenous nucleic acid which alters the expression of a vacuolar pyrophosphatase and a Na<sup>+</sup>/H<sup>+</sup> antiporter.

Barkla et al. teach that plant Na<sup>+</sup>/H<sup>+</sup> antiporters can transport Na<sup>+</sup> into the vacuole using the proton electrochemical gradient generated by vacuolar pyrophosphatase, and that a role for Na<sup>+</sup>/H<sup>+</sup> antiport in the ability of plants to tolerate salt is indicated in a number of plant species (page 550 column 1 first paragraph).

Sarafian et al. teach an exogenous nucleic acid encoding the *Arabidopsis* vacuolar pyrophosphatase AVP1 which can alter the expression of a vacuolar pyrophosphatase (page 1777 Figure 2).

Nass et al. teach an exogenous nucleic acid encoding the yeast Na<sup>+</sup>/H<sup>+</sup> antiporter NHX1, a homologue of AtNHX1, which can alter the expression of a Na<sup>+</sup>/H<sup>+</sup> antiporter, and which also confers salt tolerance in yeast (page 26149 Figure 4; page 26149 Figure 5).

The specification teaches at page 26 lines 20-22 that use of the double tandem enhancer of the 35S promoter of CaMV in plant transformation constructs was known in the art prior to Applicant's invention.

Given the success of Sheveleva et al. in improving plant salt tolerance by transforming plants with an exogenous nucleic acid encoding a protein involved in salt tolerance, and given the teachings of Barkla et al. and Nass et al. that  $\text{Na}^+/\text{H}^+$  antiporters and vacuolar pyrophosphatases are involved in salt tolerance, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to transform a plant with exogenous nucleic acids encoding both an  $\text{Na}^+/\text{H}^+$  antiporter such as NHX1 taught by Nass et al., and a vacuolar pyrophosphatase such as AVP1 taught by Sarafian et al., for the purpose of making transgenic plants that are salt tolerant, especially given the further teaching of Barkla et al. that plant  $\text{Na}^+/\text{H}^+$  antiporters can transport  $\text{Na}^+$  into the vacuole using the proton electrochemical gradient generated by vacuolar pyrophosphatase, without any surprising or unexplained results. Furthermore, the use of the double tandem enhancer of the 35S promoter of CaMV would have been an obvious modification of design parameters. Accordingly, one skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

#### ***Remarks***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC  
December 10, 2003



ASHWIN D. MEHTA, PH.D  
PATENT EXAMINER